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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,882	12/07/2005	Armin Prasch	SMB-PT164 (PC 04 246 K US	2925

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EXAMINER	
WESTERBERG, NISSA M	

ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,882	PRASCH ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 March 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 20* is/are pending in the application.

4a) Of the above claim(s) *10, 13, 15 - 20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 9, 11, 12, 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed March 30, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1 – 3, 7 – 9, 11, 12 and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al. (US 2002/0102294) in view of Remington (2000) an Uhlemann et al. (US 4,946,654). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 30, 2008 and those set forth below.

Applicant traverses this rejection on the grounds that the particles formed by the method of Bosch by spray drying would have very irregular shapes and are limited to sizes much smaller than those of Applicant's method. The residence time in the apparatus is much too short for defined granulation such as that recited in Applicant's claims. During freeze drying, only the solid material present in each droplet is found in the final particle. This results in irregular or hollow particles which are fragile, cohesive and have sizes usually on the scale of micrometers. Spray granulation is only used for "forming starting seeds for palletizing" as part of a greater process, which Bosch fails to teach. The particles produced by the claimed process have regular shapes, high flowability and compact layer structures. The method of Bosch is directed towards producing aerosols for inhalation and as the disclosure is limited this application and teaches away from its modification to include a fluidized bed apparatus as this would produce particle too large for Bosch's purpose.

In regards to Remington, Applicant argues that even if the references were combinable, Remington fails to teach or suggest injecting the liquid dispersion into a fluidized bed device and fails to teach or suggest a homogenous suspension of at least one micronized effective agent in water". The liquid suspensions and the use of suspending agents are discussed as final products, not starting materials.

In regards to Uhlemann, the instant claims require the use of micronized particles of the effective agents as starting materials, which this reference fails to teach or suggest. There is no motivation to combine these references absent impermissible hindsight.

There arguments are not found persuasive. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a

reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). It is unclear, in the absence of more specific arguments by Applicant, why it would not be obvious to consult references such as Remington and Uhlemann et al. for more detailed information in order to carry out the process described by Bosch et al. Bosch et al. teaches a generalized process for the preparation of powders containing microparticles (¶¶ [0025] – [0027]), but provides few details as to the particular steps or equipment one would employ to carry out the method. Remington and Uhlemann each provide more information about the type of equipment and how the process is carried out.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The various aspects that each reference fails to teach are taught by other references and therefore the teachings of the cited prior art in combination with each other as whole, and not the lacking of any particular reference, must be considered. The micronized effective agent starting material is taught by Bosch et al. Bosch et al. is silent as to the type of apparatus used to accomplish the spray drying process, which can be accomplished in a fluidized bed apparatus. The particle size can be varied based on the operating parameters and Applicant has not provided any evidence that the products described by Bosch et al. cannot be prepared by such a method. The failure of Bosch to explicitly mention this apparatus is not a teaching away from using

this apparatus. While Remington may discuss suspensions as final products and not as components for further processing, Bosch et al. teaches that the same type of composition, namely an aqueous dispersions, can be used as starting materials for the production of various pharmaceutical products that are injected into a fluidized bed device, such as that described by Uhlemann et al.

In regards to physical properties of the particles produced, the instant claims do not contain limitations regarding particle fragility, particle flowability or the compact layer structure. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant has not presented any evidence that the materials used or formed during the steps of the cited prior art do not fall within the scope of the instant claims. Arguments without factual support are mere allegations and not found to be persuasive. Dependent claim 3 does require the effective agent be provided in a micronized form with a grain size of less than 30 µm but as discussed in greater detail on p 3 of the October 30, 2008 Office Action, this size limitation is met by the starting material disclosed by Bosch et al. The particles produced by Bosch et al. are about 1 micron to about 2 microns in size (¶ [0026], which falls with in the range of particle sizes of 0.1 – 500 microns recited in instant claim 12. Claim 12 also required "spherical" micropellets but Applicant has not presented any evidence that these particles of Bosch et al. do not meet this limitation. Residence time in the apparatus is not recited in the instant claims. The injection of the liquid dispersion result in the formation of particles which applicant labels as "starter seeds for pelletizing by spray

granulation of the dispersion". The same steps result in what Bosch et al. terms a powder but "starter seed" or "powder" are merely labels applied to the same material as the same steps were used to produce it. "For pelletizing by spray granulation of the dispersion" is a recitation of intended use of the starter seeds. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Bosch et al. does not indicate that these materials could granulated, these materials are capable of being granulated and therefore this claim limitation is met. Claim 14 only requires further processing of the pellets into a pharmaceutical formulation. This step could simple be met by the packaging of the produced material into container(s) that are dispensed to a patient.

5. Claims 1 – 4, 7 - 9, 11, 12 and 14 were rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., Remington and Uhlemann further in view of Liversidge et al. (US 5,145,684). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 30, 2008 and those set forth below.

Applicant traverses this rejection on the grounds that Liversidge describes the manufacture of liquid formulations and only very generally states that such dispersions can be spray dried or used in a fluid bed dryer to coat cores. Claim 1 requires the fluidized bed device to be "initially free from core-forming substances".

These arguments are not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Bosch et al. does not describe the use polyoxypropylene-polyoxyethylene as a functional adjuvant in the dispersion. Liversidge describes the use of this compound in solution of submicron sized particles in liquid to alter the interactions of the particles in a desirable way. While the intended use of these solutions may be different, the aggregation issues will be the same and therefore can be dealt with using the same strategies, namely the inclusions of solutizers such as polyvinylpyrrolidone (PVP), which is described by both Bosch et al. and Liversidge et al., or polyoxypropylene-polyoxyethylene polymers, which are only described by Liversidge et al.

6. Claims 1 – 3, 5 – 9, 11, 12 and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Bosch et al., Remington, Uhlemann et al. and Liversidge et al. further in view of Appel et al. (EP 1027867). This rejection is MAINTAINED for the reasons of record set forth in the Office Action mailed October 30, 2008 and those set forth below.

Applicant traverses this rejection on the grounds that Appel's disclosure focuses on spray-drying, which is different from the method of, and would not lead to appropriate micropellets. The drug is not added in micronized form. The fact that clarithromycin is incidentally mentioned does not provide any incentive to combine with the other cited references to arrive at Applicants' claimed method.

These arguments are not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). The failure of Appel et al. to use a micronized starting material is not relevant as this teaching is found in the other applied references.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re*

Jones, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, Appel discloses clarithromycin to be a low solubility drug that thus decreases its bioavailability. Taken in conjunction with the other applied references, Liversidge et al. discloses that the bioavailability of such compounds, such as antibiotics (col 3, ln 56), can be increased by formulation of such low solubility ingredients with solutizers, while Bosch et al., Remington and Uhlemann et al. describe the steps by which such materials can be prepared by one wishing to prepare a pharmaceutical preparation of clarithromycin. Thus the desirability of small particle formulations with solutizers are the steps by which such compositions can be prepared are disclosed by the cited prior art.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW